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Amendments to the Claims:

1. (Currently Amended): A method for treating or preventing reducing the risk of arthritis in a mammal, said method comprising the step of administering to a patient suffering from arthritis and in need of treatment, or to a patient suspected of developing arthritis, an effective antiarthritic amount of a MEK inhibitor.

B 1

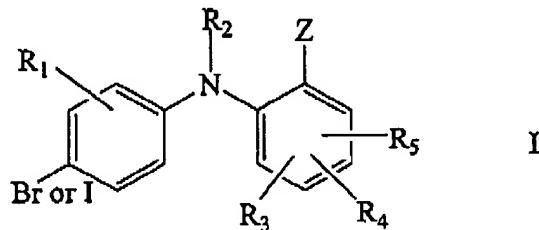
2. (Original): The method according to Claim 1 wherein the arthritis is rheumatoid arthritis or osteoarthritis.

3. (Original): The method according to Claim 2, wherein the arthritis is osteoarthritis.

4. (Original): The method according to Claim 2, wherein the arthritis is rheumatoid arthritis.

5. (Original): The method according to Claim 1, wherein said MEK inhibitor is a selective MEK1 or MEK 2 inhibitor.

6. (Previously Amended): The method according to Claim 1 wherein the MEK inhibitor is a compound of Formula I



wherein:

R₁ is hydrogen, hydroxy, C₁-C₈ alkyl, C₁-C₈ alkoxy, halo, trifluoromethyl, or CN;

R₂ is hydrogen;

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Cont

R₃, R₄, and R₅ independently are hydrogen, hydroxy, halo, trifluoromethyl, C₁-C₈ alkyl, C₁-C₈ alkoxy, nitro, CN, or -(O or NH)_m-(CH₂)_n-R₉, where R₉ is hydrogen, hydroxy, COOH, or NR₁₀R₁₁;

n is 0-4;

m is 0 or 1;

R₁₀ and R₁₁ independently are hydrogen or C₁-C₈ alkyl, or taken together with the nitrogen to which they are attached can complete a 3-10 member cyclic ring optionally containing 1, 2, or 3 additional heteroatoms selected from O, S, NH, or N-C₁-C₈ alkyl;

Z is COOR₇, tetrazolyl, CONR₅R₇, CONHNR₁₀R₁₁, or CH₂OR₇;

R₆ and R₇ independently are hydrogen, C₁-C₈ alkyl, C₂-C₈ alkenyl, C₂-C₈ alkynyl, (CO)-C₁-C₈ alkyl, aryl, heteroaryl, or C₃-C₁₀ cycloalkyl optionally containing one, two, or three heteroatoms selected from O, S, NH, or N alkyl; or R₆ and R₇ together with the nitrogen to which they are attached complete a 3-10 member cyclic ring optionally containing 1,2, or 3 additional heteroatoms selected from O, S, NH, or N alkyl; and wherein any of the foregoing alkyl, alkenyl, aryl, heterocyclic, and alkynyl groups can be unsubstituted or substituted by halo, hydroxy, C₁-C₆ alkoxy, amino, nitro, C₁-C₄ alkylamino, di(C₁-C₄) alkylamino, C₃-C₆ cycloalkyl, phenyl, phenoxy, C₃-C₅ heteroaryl, or C₃-C₅ heteroaryloxy;

or a pharmaceutically acceptable salt, ester, amide, or prodrug thereof.

7. (Original): The method according to Claim 6 wherein the MEK inhibitor is a compound selected from:

[4-Chloro-2-(1H-tetrazol-5-yl)-phenyl-(4-iodo-2-methyl-phenyl)-amine;
(4-iodo-2-methyl-phenyl)-[2-(1H-tetrazol-5-yl)-phenyl]amine;
[4-nitro-2-(1H-tetrazol-5-yl)-phenyl-(4-iodo-2-methyl-phenyl)-amine;

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4-Fluoro-2-(4-iodo-2-methylphenylamino)benzoic acid;
3,4,5-Trifluoro-2-(4-iodo-2-methyl-phenylamino)-benzoic acid;
3,4-Difluoro-2-(4-iodo-2-methyl-phenylamino)-benzoic acid;
5-Bromo-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-benzoic acid;
5-Chloro-2-(4-iodo-2-methyl-phenylamino)-benzoic acid;
Sodium 5-Chloro-2-(4-iodo-2-methyl-phenylamino)-benzoate;
5-Bromo-2-(4-iodo-2-methyl-phenylamino)-benzoic acid;
2-(4-Iodo-2-methyl-phenylamino)-5-nitro-benzoic acid;
4-Chloro-2-(4-iodo-2-methyl-phenylamino)-benzoic acid;
2-(4-Iodo-2-methyl-phenylamino)-benzoic acid;
5-Fluoro-2-(4-iodo-2-methyl-phenylamino)-benzoic acid;
5-Iodo-2-(4-iodo-2-methyl-phenylamino)-benzoic acid;
2,3,5-Trifluoro-4-(4-iodo-2-methyl-phenylamino)-benzoic acid;
2-(4-Iodo-phenylamino)-5-methoxy-benzoic acid;
5-Methyl-2-(4-iodo-2-methyl-phenylamino)-benzoic acid;
2-(4-Iodo-2-methyl-phenylamino)-4-nitro-benzoic acid;
2-(4-Bromo-2-methyl-phenylamino)-4-fluoro-benzoic acid;
2-(2-Bromo-4-iodo-phenylamino)-5-nitro-benzoic acid;
2-(4-Bromo-2-methyl-phenylamino)-3,4-difluoro-benzoic acid;
5-Chloro-N-(2-hydroxyethyl)-2-(4-iodo-2-methyl-phenylamino)-benzamide;
4-Fluoro-2-(4-iodo-2-methyl-phenylamino)-benzamide;
4-Fluoro-2-(4-iodo-2-methyl-phenylamino)-N-methyl-benzamide;
N-Ethyl-4-fluoro-2-(4-iodo-2-methyl-phenylamino)-benzamide;
4-Fluoro-2-(4-iodo-2-methyl-phenylamino)-N,N-dimethyl-benzamide;
4-Fluoro-2-(4-iodo-2-methyl-phenylamino)-N-(1H-tetrazol-5-yl)-benzamide;
5-Bromo-2-(4-iodo-2-methyl-phenylamino)-benzamide;
5-Chloro-2-(4-iodo-2-methyl-phenylamino)-N,N-dimethyl-benzamide;
[5-Chloro-2-(4-iodo-2-methyl-phenylamino)-benzoyl]amino]-acetic acid;
4-Fluoro-2-(4-iodo-2-methyl-phenylamino)-N-propyl-benzamide;
5-Bromo-N-(2-hydroxy-ethyl)-2-(4-iodo-2-methyl-phenylamino)-benzamide;
N,N-Diethyl-4-fluoro-2-(4-iodo-2-methyl-phenylamino)-benzamide;

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4-Fluoro-N-{3-[4-(2-hydroxy-ethyl)-piperazin-1-yl]-propyl}-2-(4-iodo-2-methyl-phenylamino)-benzamide;
N,N-Diethyl-2-(4-iodo-2-methyl-phenylamino)-5-nitro-benzamide;
N-Butyl-4-fluoro-2-(4-iodo-2-methyl-phenylamino)-benzamide;
5-Chloro-N,N-diethyl-2-(4-iodo-2-methyl-phenylamino)-benzamide;
5-Bromo-2-(4-iodo-2-methyl-phenylamino)-N,N-dimethyl-benzamide;
5-Bromo-3,4-difluoro-N-(2-hydroxy-ethyl)-2-(4-iodo-2-methyl-phenylamino)-benzamide;
N-(2,3-Dihydroxy-propyl)-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-benzamide;
5-Bromo-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-N-(2-piperidin-1-yl-ethyl)-benzamide;
3,4-Difluoro-N-(2-hydroxy-ethyl)-2-(4-iodo-2-methyl-phenylamino)-benzamide;
N-(2,3-Dihydroxy-propyl)-4-fluoro-2-(4-iodo-2-methyl-phenylamino)-benzamide;
3,4-Difluoro-N-(3-hydroxy-propyl)-2-(4-iodo-2-methyl-phenylamino)-benzamide;
5-Bromo-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-N-(2-pyrrolidin-1-yl-ethyl)-benzamide;
5-Bromo-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-N-(2-pyridin-4-yl-ethyl)-benzamide;
4-Fluoro-N-(2-hydroxy-ethyl)-2-(4-iodo-2-methyl-phenylamino)-benzamide;
5-Bromo-N-(3-dimethylamino-propyl)-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-benzamide;
5-Bromo-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-N-(2-morpholin-4-yl-ethyl)-benzamide;
3,4-Difluoro-2-(4-iodo-2-methyl-phenylamino)-N-(2-morpholin-4-yl-ethyl)-benzamide;
3,4-Difluoro-2-(4-iodo-2-methyl-phenylamino)-N-(2-pyrrolidin-1-yl-ethyl)-benzamide;
3,4-Difluoro-2-(4-iodo-2-methyl-phenylamino)-N-(2-pyridin-4-yl-ethyl)-benzamide;
N-(3-Dimethylamino-propyl)-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-benzamide;
N-Benzyl-4-fluoro-2-(4-iodo-2-methyl-phenylamino)-benzamide;
2-(4-Bromo-2-methyl-phenylamino)-3,4-difluoro-N-(2-hydroxy-ethyl)-benzamide;
4-Fluoro-2-(4-iodo-2-methyl-phenylamino)-N-(2-morpholin-4-yl-ethyl)-benzamide;

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4-Fluoro-2-(4-iodo-2-methyl-phenylamino)-N-(3-piperidin-1-yl-propyl)-benzamide;
3,4-Difluoro-2-(4-iodo-2-methyl-phenylamino)-N-(3-piperidin-1-yl-propyl)-benzamide;
4-Fluoro-2-(4-iodo-2-methyl-phenylamino)-N-(2-thiophen-2-yl-ethyl)-benzamide;
4-Fluoro-2-(4-iodo-2-methyl-phenylamino)-N-(2-pyrrolidin-1-yl-ethyl)-benzamide;
2-(4-Bromo-2-methyl-phenylamino)-3,4-difluoro-N-(2-morpholin-4-yl-ethyl)-
benzamide;
5-Bromo-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-N-pyridin-4-ylmethyl-
benzamide;
3,4-Difluoro-2-(4-iodo-2-methyl-phenylamino)-N-pyridin-4-ylmethyl-benzamide;
2-(4-Bromo-2-methyl-phenylamino)-N-(3-dimethylamino-propyl)-3,4-difluoro-
benzamide;
4-Fluoro-2-(4-iodo-2-methyl-phenylamino)-N-pyridin-4-ylmethyl-benzamide;
4-Fluoro-2-(4-iodo-2-methyl-phenylamino)-N-(2-pyridin-4-yl-ethyl)-benzamide;
2-(4-Bromo-2-methyl-phenylamino)-3,4-difluoro-N-(2-pyridin-4-yl-ethyl)-benzamide;
2-(4-Bromo-2-methyl-phenylamino)-3,4-difluoro-N-(3-hydroxy-propyl)-benzamide;
2-(4-Bromo-2-methyl-phenylamino)-3,4-difluoro-N-(2-pyrrolidin-1-yl-ethyl)-
benzamide;
4-Fluoro-2-(4-iodo-2-methyl-phenylamino)-N-phenethyl-benzamide;
2-(4-Bromo-2-methyl-phenylamino)-3,4-difluoro-N-(2-thiophen-2-yl-ethyl)-benzamide;
2-(4-Bromo-2-methyl-phenylamino)-3,4-difluoro-N-pyridin-4-ylmethyl-benzamide;
2-(4-Bromo-2-methyl-phenylamino)-3,4-difluoro-N-phenethyl-benzamide;
2-(4-Bromo-2-methyl-phenylamino)-3,4-difluoro-N-(2-piperidin-1-yl-ethyl)-benzamide;
5-Chloro-N-{3-[4-(2-hydroxy-ethyl)-piperazin-1-yl]-propyl}-2-(4-iodo-2-methyl-
phenylamino)- benzamide;
5-Fluoro-N-{3-[4-(2-hydroxy-ethyl)-piperazin-1-yl]-propyl}-2-(4-iodo-2-methyl-
phenylamino)- benzamide;
2-(4-Iodo-2-methyl-phenylamino)-5-nitro-N-pyridin-4-yl methyl-benzamide;
5-Bromo-N-{3-[4-(2-hydroxy-ethyl)-piperazin-1-yl]-propyl}-2-(4-iodo-2-methyl-
phenylamino)- benzamide;
5-Chloro-N-(2-diethylamino-ethyl)-2-(4-iodo-2-methyl-phenylamino)- benzamide;
5-Chloro-2-(4-iodo-2-methyl-phenylamino)-N-(2-piperidin-1-yl-ethyl)-benzamide;

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(3-Hydroxy-pyrrolidin-1-yl)-[2-(4-iodo-2-methyl-phenylamino)-5-nitro-phenyl]-methanone;

5-Chloro-2-(4-iodo-2-methyl-phenylamino)-N-(2-pyrrolidin-1-yl-ethyl)-benzamide;

5-Bromo-N-(2-diethylamino-ethyl)-2-(4-iodo-2-methyl-phenylamino)-benzamide;

N-{2-[Bis-(2-hydroxy-ethyl)-amino]-ethyl}-5-chloro-2-(4-iodo-2-methyl-phenylamino)-benzamide;

N-{2-[Bis-(2-hydroxy-ethyl)-amino]-ethyl}-5-bromo-2-(4-iodo-2-methyl-phenylamino)-benzamide;

N-{3-[4-(2-Hydroxy-ethyl)-piperazin-1-yl]-propyl}-2-(4-iodo-2-methyl-phenylamino)-benzamide;

5-Fluoro-2-(4-iodo-2-methyl-phenylamino)-N-pyridin-4-ylmethyl-benzamide;

5-Bromo-2-(4-iodo-2-ethyl-phenylamino)-N-(2-pyrrolidin-1-yl-ethyl)-benzamide;

5-Bromo-2-(4-iodo-2-methyl-phenylamino)-N-(2-piperidin-1-yl-ethyl)-benzamide;

5-Fluoro-2-(4-iodo-2-methyl-phenylamino)-N-(2-pyrrolidin-1-yl-ethyl)-benzamide;

5-Chloro-N-(3-dimethylamino-propyl)-2-(4-iodo-2-methyl-phenylamino)-benzamide;

N-{2-[Bis-(2-hydroxy-ethyl)-amino]-ethyl}-5-fluoro-2-(4-iodo-2-methyl-phenylamino)-benzamide;

5-Chloro-N-(3-hydroxy-propyl)-2-(4-iodo-2-methyl-phenylamino)-benzamide;

5-Chloro-N-(3-diethylamino-2-hydroxy-propyl)-2-(4-iodo-2-methyl-phenylamino)-benzamide;

5-Fluoro-2-(4-iodo-2-methyl-phenylamino)-N-(2-piperidin-1-yl-ethyl)-benzamide;

5-Bromo-N-(3-hydroxy-propyl)-2-(4-iodo-2-methyl-phenylamino)-benzamide;

5-Bromo-2-(4-iodo-2-methyl-phenylamino)-N-(3-piperidin-1-yl-propyl)-benzamide;

N-{2-[Bis-(2-hydroxy-ethyl)-amino]-ethyl}-2-(4-iodo-2-methyl-phenylamino)-5-nitro-benzamide;

5-Chloro-2-(4-iodo-2-methyl-phenylamino)-N-(2-morpholin-4-yl-ethyl)-benzamide;

5-Chloro-N-(3-diethylamino-propyl)-2-(4-iodo-2-methyl-phenylamino)-benzamide;

5-Chloro-N-(2-diisopropylamino-ethyl)-2-(4-iodo-2-methyl-phenylamino)-benzamide;

5-Chloro-2-(4-iodo-2-methyl-phenylamino)-N-(3-piperidin-1-yl-propyl)-benzamide;

2-(4-Iodo-2-methyl-phenylamino)-5-nitro-N-(2-piperidin-1-yl-ethyl)-benzamide;

5-Bromo-2-(4-iodo-2-methyl-phenylamino)-N-(2-piperazin-1-yl-ethyl)-benzamide;

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N-(2-Diethylamino-ethyl)-5-fluoro-2-(4-iodo-2-methyl-phenylamino)-benzamide;
5-Bromo-N-(3-dimethylamino-propyl)-2-(4-iodo-2-methyl-phenylamino)-benzamide;
N-(3-Hydroxy-propyl)-2-(4-iodo-2-methyl-phenylamino)-5-nitro-benzamide;
5-Fluoro-N-(3-hydroxy-propyl)-2-(4-iodo-2-methyl-phenylamino)-benzamide;
N-(3-Diethylamino-propyl)-5-fluoro-2-(4-iodo-2-methyl-phenylamino)-benzamide;
N-(3-Diethylamino-propyl)-2-(4-iodo-2-methyl-phenylamino)-5-nitro-benzamide;
5-Bromo-2-(4-iodo-2-methyl-phenylamino)-N-(2-morpholin-4-yl-ethyl)-benzamide;
2-(4-Iodo-2-methyl-phenylamino)-5-nitro-N-(3-piperidin-1-yl-propyl)-benzamide;
[5-Fluoro-2-(4-iodo-2-methyl-phenylamino)-phenyl]-[3-hydroxy-pyrrolidin-1-yl]-
methanone;
5-Bromo-N-(2-diisopropylamino-ethyl)-2-(4-iodo-2-methyl-phenylamino)-benzamide;
5-Fluoro-2-(4-iodo-2-methyl-phenylamino)-N-(2-morpholin-4-yl-ethyl)-benzamide;
5-Fluoro-2-(4-iodo-2-methyl-phenylamino)-N-(3-piperidin-1-yl-propyl)-benzamide;
[5-Fluoro-2-(4-iodo-2-methyl-phenylamino)-phenyl]-[4-(2-hydroxy-ethyl)-piperazin-1-
yl]-methanone;
N-(3-Diethylamino-2-hydroxy-propyl)-5-fluoro-2-(4-iodo-2-methyl-phenylamino)-
benzamide;
N-Cyclopropyl-5-fluoro-2-(4-iodo-2-methyl-phenylamino)-benzamide;
5-Chloro-N-(2-hydroxy-ethyl)-2-(4-iodo-2-methyl-phenylamino)-benzamide;
5-Fluoro-N-(2-hydroxy-ethyl)-2-(4-iodo-2-methyl-phenylamino)-benzamide;
N-Benzyl-5-fluoro-2-(4-iodo-2-methyl-phenylamino)-benzamide;
N-Benzyl-5-bromo-2-(4-iodo-2-methyl-phenylamino)-benzamide;
2-(4-Iodo-2-methyl-phenylamino)-5-nitro-N-(4-sulfamoyl-benzyl)-benzamide;
5-Bromo-N-(2-hydroxy-ethyl)-2-(4-iodo-2-methyl-phenylamino)-benzamide;
N-(2-Hydroxy-ethyl)-5-iodo-2-(4-iodo-2-methyl-phenylamino)-benzamide;
N-(2-Hydroxy-ethyl)-2-(4-iodo-2-ethyl-phenylamino)-5-nitro-benzamide;
2-(4-Iodo-2-methyl-phenylamino)-N-methyl-5-nitro-N-phenyl-benzamide;
5-Chloro-N-cyclopropyl-2-(4-iodo-2-methyl-phenylamino)-benzamide;
5-Fluoro-2-(4-iodo-2-methyl-phenylamino)-N-methyl-N-phenyl-benzamide;
N-Allyl-5-fluoro-2-(4-iodo-2-methyl-phenylamino)-benzamide;
N-Benzyl-5-iodo-2-(4-iodo-2-methyl-phenylamino)-benzamide;

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5-Fluoro-2-(4-iodo-2-methyl-phenylamino)-N-(4-sulfamoyl-benzyl)-benzamide;
N-Allyl-5-chloro-2-(4-iodo-2-methyl-phenylamino)-benzamide;
N-Cyclopropyl-2-(4-iodo-2-methyl-phenylamino)-5-nitro-benzamide;
5-Bromo-N-cyclopropyl-2-(4-iodo-2-methyl-phenylamino)-benzamide;
5-Chloro-2-(4-iodo-2-methyl-phenylamino)-N-methyl-N-phenyl-benzamide;
5-Iodo-2-(4-iodo-2-methyl-phenylamino)-N-(4-sulfamoyl-benzyl)-benzamide;
5-Bromo-2-(4-iodo-2-methyl-phenylamino)-N-(4-sulfamoyl-benzyl)-benzamide;
N-Allyl-2-(4-iodo-2-methyl-phenylamino)-5-nitro-benzamide; 2-(4-Iodo-2-methyl-phenylamino)-5-nitro-N-(4-sulfamoyl-benzyl)-benzamide;
N-Allyl-5-bromo-2-(4-iodo-2-methyl-phenylamino)-benzamide;
5-Fluoro-2-(4-iodo-2-methyl-phenylamino)-N-(3-methyl-benzyl)-benzamide;
N-Cyclopropyl-5-iodo-2-(4-iodo-2-methyl-phenylamino)-benzamide;
5-Bromo-2-(4-iodo-2-methyl-phenylamino)-N-methyl-N-phenyl-benzamide;
N-Benzyl-2-(4-iodo-2-methyl-phenylamino)-5-nitro-benzamide;
N-Cyclohexyl-5-iodo-2-(4-iodo-2-methyl-phenylamino)-benzamide;
N-Allyl-5-iodo-2-(4-iodo-2-methyl-phenylamino)-benzamide;
5-Iodo-2-(4-iodo-2-methyl-phenylamino)-N-(3-methyl-benzyl)-benzamide;
2-(4-Iodo-2-methyl-phenylamino)-N-(3-methyl-benzyl)-5-nitro-benzamide;
5-Iodo-2-(4-iodo-2-methyl-phenylamino)-N-methyl-N-phenyl-benzamide;
N-Cyclohexyl-5-fluoro-2-(4-iodo-2-methyl-phenylamino)-benzamide;
5-Chloro-N-cyclohexyl-2-(4-iodo-2-methyl-phenylamino)-benzamide;
5-Bromo-2-(4-iodo-2-methyl-phenylamino)-N-(3-methyl-benzyl)-benzamide;
5-Bromo-N-cyclohexyl-2-(4-iodo-2-methyl-phenylamino)-benzamide;
5-Chloro-2-(4-iodo-2-methyl-phenylamino)-N-(3-methyl-benzyl)-benzamide;
N-Cyclohexyl-2-(4-iodo-2-methyl-phenylamino)-5-nitro-benzamide;
N-Benzyl-2-(4-iodo-2-methyl-phenylamino)-benzamide;
N-Benzyl-5-bromo-2-(4-iodo-2-methyl-phenylamino)-benzamide;
N-Benzyl-5-fluoro-2-(4-iodo-2-methyl-phenylamino)-benzamide;
5-Chloro-N-(2-hydroxy-ethyl)-2-(4-iodo-2-methyl-phenylamino)-benzamide;
5-Bromo-N-(2-hydroxy-ethyl)-2-(4-iodo-2-methyl-phenylamino)-benzamide;
2-(4-Iodo-2-methyl-phenylamino)-N-methyl-5-nitro-N-phenyl-benzamide;

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5-Chloro-2-(4-iodo-2-methyl-phenylamino)-N-methyl-N-phenyl-benzamide;
N-(2-Hydroxy-ethyl)-5-iodo-2-(4-iodo-2-methyl-phenylamino)-benzamide;
5-Chloro-N-cyclopropyl-2-(4-iodo-2-methyl-phenylamino)-benzamide;
N-Allyl-5-chloro-2-(4-iodo-2-methyl-phenylamino)-benzamide;
5-Fluoro-2-(4-iodo-2-methyl-phenylamino)-N-methyl-N-phenyl-benzamide;
N-(2-Hydroxy-ethyl)-2-(4-iodo-2-methyl-phenylamino)-5-nitro-benzamide;
5-Fluoro-N-(2-hydroxy-ethyl)-2-(4-iodo-2-methyl-phenylamino)-benzamide;
5-Bromo-N-cyclopropyl-2-(4-iodo-2-methyl-phenylamino)-benzamide;
N-Cyclopropyl-5-fluoro-2-(4-iodo-2-methyl-phenylamino)-benzamide;
5-Fluoro-2-(4-iodo-2-methyl-phenylamino)-N-(4-sulfamoyl-benzyl)-benzamide;
N-Cyclopropyl-2-(4-iodo-2-methyl-phenylamino)-5-nitro-benzamide;
N-Allyl-5-fluoro-2-(4-iodo-2-methyl-phenylamino)-benzamide;
N-Benzylxy-5-ido-2-(4-ido-2-methyl-phenylamino)-benzamide;
N-Allyl-5-bromo-2-(4-ido-2-methyl-phenylamino)-benzamide;
5-Bromo-2-(4-ido-2-methyl-phenylamino)-N-(4-sulfamoyl-benzyl)-benzamide;
5-Bromo-2-(4-ido-2-methyl-phenylamino)-N-methyl-N-phenyl-benzamide;
N-Allyl-2-(4-ido-2-methyl-phenylamino)-5-nitro-benzamide;
4-Fluoro-2-(4-ido-2-methyl-phenylamino)-benzyl alcohol;
[5-Chloro-2-(4-ido-2-methyl-phenylamino)-phenyl]-methanol;
[2-(4-Iodo-2-methyl-phenylamino)-5-nitro-phenyl]-methanol;
[5-Bromo-2-(4-ido-2-methyl-phenylamino)-phenyl]-methanol; and
N-Allyl-2-(4-ido-2-methyl-phenylamino)-5-nitro-benzamide.

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8. (Previously Amended): The method of claim 6, wherein the MEK inhibitor is a compound of Formula (I) wherein (a) R₁ is hydrogen, methyl, methoxy, fluoro, chloro, or bromo; (b) R₂ is hydrogen; (c) R₃, R₄, and R₅ independently are hydrogen, fluoro, chloro, bromo, iodo, methyl, methoxy, or nitro; (d) R₁₀ and R₁₁ independently are hydrogen or methyl; (e) Z is COOR₇, tetrazolyl, CONR₆R₇, CONHNR₁₀R₁₁, or CH₂OR₇; R₆ and R₇ independently are hydrogen, C₁₋₄ alkyl, heteroaryl, or C₃₋₅ cycloalkyl optionally containing one or two heteroatoms selected from O, S, or NH; or R₆ and R₇ together with the nitrogen to which they are attached complete a 5-6 member cyclic ring

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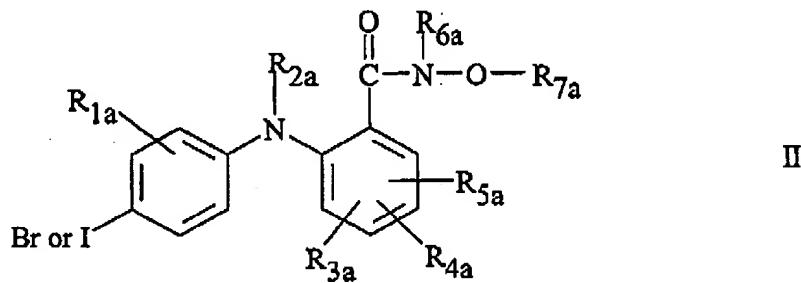
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optionally containing 1 or 2 additional heteroatoms selected from O, NH or N-alkyl; and wherein any of the foregoing alkyl or aryl groups can be unsubstituted or substituted by halo, hydroxy, methoxy, ethoxy, or heteroaryloxy.

9. (Original): The method of claim 8, wherein the MEK inhibitor is a compound of Formula (I) wherein: Z is COOR₇; R₇ is H, pentafluorophenyl, or tetrazolyl; R₃ and R₅ are independently H, fluoro, or chloro; and R₄ is fluoro.

10. (Original): The method of Claim 1 wherein the MEK inhibitor is a compound of Formula II



wherein:

R_{1a} is hydrogen, hydroxy, C₁-C₈ alkyl, C₁-C₈ alkoxy, halo, trifluoromethyl, or CN;

R_{2a} is hydrogen;

R_{3a}, R_{4a}, and R_{5a} independently are hydrogen, hydroxy, halo, trifluoromethyl,

C₁-C₈ alkyl, C₁-C₈ alkoxy, nitro, CN, or (O or NH)_m-(CH₂)_n-R_{9a}, where

R_{9a} is hydrogen, hydroxy, CO₂H or NR_{10a}R_{11a}.

n is 0-4;

m is 0 or 1;

R_{10a} and R_{11a} independently are hydrogen or C₁-C₈ alkyl, or taken together with the nitrogen to which they are attached can complete a 3- to 10-member cyclic ring optionally containing one, two, or three additional heteroatoms selected from O, S, NH, or N-C₁-C₈ alkyl;

R_{6a} is hydrogen, C₁-C₈ alkyl, (CO)-C₁-C₈ alkyl, aryl, aralkyl, or C₃-C₁₀ cycloalkyl;

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R_{7a} is hydrogen, C₁-C₈ alkyl, C₂-C₈ alkenyl, C₂-C₈ alkynyl, C₃-C₁₀ (cycloalkyl or cycloalkyl optionally containing a heteroatom selected from O, S, or NR_{9a}); and wherein any of the foregoing alkyl, alkenyl, aryl, heteroaryl, heterocyclic, and alkynyl groups can be unsubstituted or substituted by halo, hydroxy, C₁-C₆ alkoxy, amino, nitro, C₁-C₄ alkylamino, di(C₁-C₄)alkylamino, C₃-C₆ cycloalkyl, phenyl, phenoxy, C₃-C₅ heteroaryl or heterocyclic radical, or C₃-C₅ heteroaryloxy or heterocyclic radical-oxy; or R_{6a} and R_{7a} taken together with the N to which they are attached can complete a 5- to 10-membered cyclic ring, optionally containing one, two, or three additional heteroatoms selected from O, S, or NR_{10a}R_{11a}; or a pharmaceutically acceptable salt, ester, amide or prodrug thereof.

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Cont

11. (Original): The method of Claim 10, comprising a MEK inhibitor having a structure of Formula (II) wherein: (a) R_{1a} is H, methyl, fluoro, or chloro; (b) R_{2a} is H; R_{3a}, R_{4a}, and R_{5a} are each H, Cl, nitro, or F; (c) R_{6a} is H; (d) R_{7a} is methyl, ethyl, 2-propenyl, propyl, butyl, pentyl, hexyl, cyclopropylmethyl, cyclobutyl methyl, cyclopropylmethyl, or cyclopropylethyl; and (e) the 4' position is I, rather than Br.

12. (Original): The method of claim 11, comprising a MEK inhibitor having a structure of Formula (II) wherein: R_{4a} is F at the 4 position, para to the CO-N-R_{6a}-OR_{7a} group and meta to the bridging nitrogen; at least one of R_{3a} and R_{5a} is F or Cl; and R_{1a} is methyl or chloro.

13. (Original): The method of Claim 10, comprising a MEK inhibitor having a formula selected from:

4-Fluoro-N-hydroxy-2-(4-ido-2-methyl-phenylamino)-benzamide;
4-Fluoro-2-(4-ido-2-methyl-phenylamino)-N-(methoxy)-benzamide;
4-Fluoro-2-(4-ido-2-methyl-phenylamino)-N-(prop-2-ynyl)-benzamide;
4-Fluoro-2-(4-ido-2-methyl-phenylamino)-N-(2-phenoxyethoxy)-benzamide;
4-Fluoro-2-(4-ido-2-methyl-phenylamino)-N-(2-thienylmethoxy)-benzamide;

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4-Fluoro-2-(4-iodo-2-methyl-phenylamino)-N-(prop-2-enoxy)-benzamide;
4-Fluoro-2-(4-iodo-2-methyl-phenylamino)-N-(cyclopropylmethoxy)-benzamide;
4-Fluoro-2-(4-iodo-2-methyl-phenylamino)-N-(cyclopentoxy)-benzamide;
3,4-Difluoro-2-(4-iodo-2-methyl-phenylamino)-N-(3-furylmethoxy)-benzamide;
3,4-Difluoro-2-(4-iodo-2-methyl-phenylamino)-N-ethoxy-benzamide;
3,4-Difluoro-2-(4-iodo-2-methyl-phenylamino)-N-(but-2-enoxy)-benzamide;
3,4-Difluoro-2-(4-iodo-2-methyl-phenylamino)-N-(cyclopropylmethoxy)-benzamide;
3,4-Difluoro-2-(4-iodo-2-methyl-phenylamino)-N-(1-methylprop-2-nyloxy)-
benzamide;
3,4-Difluoro-2-(4-iodo-2-methyl-phenylamino)-N-(3-phenylprop-2-nyloxy)-
benzamide;
3,4-Difluoro-2-(4-iodo-2-methyl-phenylamino)-N-(3-methyl-5-phenylpent-2-en-
4-nyloxy)-benzamide;
3,4-Difluoro-2-(4-iodo-2-methyl-phenylamino)-N-(prop-2-nyloxy)-benzamide;
3,4-Difluoro-2-(4-iodo-2-methyl-phenylamino)-N-(propoxy)-benzamide;
3,4-Difluoro-2-(4-iodo-2-methyl-phenylamino)-N-(cyclobutyloxy)-benzamide;
3,4-Difluoro-2-(4-iodo-2-methyl-phenylamino)-N-(2-thienylmethoxy)-benzamide;
3,4-Difluoro-2-(4-iodo-2-methyl-phenylamino)-N-(2-methyl-prop-2-enoxy)-
benzamide;
3,4-Difluoro-2-(4-iodo-2-methyl-phenylamino)-N-(2-phenoxyethoxy)-benzamide;
3,4-Difluoro-2-(4-iodo-2-methyl-phenylamino)-N-(but-2-enoxy)-benzamide;
3,4-Difluoro-2-(4-iodo-2-methyl-phenylamino)-N-(but-3-nyloxy)-benzamide;
3,4-Difluoro-2-(4-iodo-2-methyl-phenylamino)-N-(cyclopentyloxy)-benzamide;
3,4-Difluoro-2-(4-iodo-2-methyl-phenylamino)-N-(3-(2-fluorophenyl)-prop-2-nyloxy)-
benzamide;
5-Bromo-3,4-difluoro-N-hydroxy-2-(4-iodo-2-methyl-phenylamino)-benzamide;
5-Bromo-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-N-(n-propoxy)-benzamide;
5-Bromo-3,4-difluoro-N-(furan-3-ylmethoxy)-2-(4-iodo-2-methyl-phenylamino)-
benzamide;
5-Bromo-N-(but-2-enoxy)-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-benzamide
5-Bromo-N-butoxy-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-benzamide;

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5-Bromo-3,4-difluoro-2-(4-ido-2-methyl-phenylamino)-N-(3-methyl-but-2-enoxy)-benzamide;
5-Bromo-3,4-difluoro-2-(4-ido-2-methyl-phenylamino)-N-(3-methyl-pent-2-en-4-nyloxy)-benzamide;
5-Bromo-3,4-difluoro-2-(4-ido-2-methyl-benzyl)-N-[5-(3-methoxy-phenyl)-3-methyl-pent-2-en-4-nyloxy]-benzamide;
5-Bromo-3,4-difluoro-2-(4-ido-2-methyl-phenylamino)-N-(prop-2-nyloxy)-benzamide;
5-Bromo-3,4-difluoro-2-(4-ido-2-methyl-phenylamino)-N-[3-(3-methoxy-phenyl)-prop-2-nyloxy]-benzamide;
5-Bromo-3,4-difluoro-2-(4-ido-2-methyl-phenylamino)-N-(thiopen-2-ylmethoxy)-benzamide;
5-Bromo-3,4-difluoro-2-(4-ido-2-methyl-phenylamino)-N-(pyridin-3-ylmethoxy)-benzamide;
5-Bromo-3,4-difluoro-2-(4-ido-2-methyl-phenylamino)-N-(3-(2-fluorophenyl)-prop-2-nyloxy)-benzamide;
5-Bromo-3,4-difluoro-2-(4-ido-2-methyl-phenylamino)-N-(ethoxy)-benzamide;
5-Bromo-3,4-difluoro-2-(4-ido-2-methyl-phenylamino)-N-(cyclopropylmethoxy)-benzamide;
5-Bromo-3,4-difluoro-2-(4-ido-2-methyl-phenylamino)-N-(isopropoxy)-benzamide;
5-Bromo-3,4-difluoro-2-(4-ido-2-methyl-phenylamino)-N-but-3-nyloxy)-benzamide;
5-Chloro-N-hydroxy-2-(4-ido-2-methyl-phenylamino)-benzamide;
5-Chloro-2-(4-ido-2-methyl-phenylamino)-N-(tetrahydro-pyran-2-yloxy)-benzamide;
5-Chloro-2-(4-ido-2-methyl-phenylamino)-N-methoxy-benzamide;
4-Bromo-2-(4-ido-2-methyl-phenylamino)-N-phenylmethoxy-benzamide;
4-Fluoro-2-(4-ido-2-methyl-phenylamino)-N-phenylmethoxy-benzamide;
5-Fluoro-N-hydroxy-2-(4-ido-2-methyl-phenylamino)-benzamide;
5-Iodo-2-(4-ido-2-methyl-phenylamino)-N-phenylmethoxy-benzamide;
5-Fluoro-2-(4-ido-2-methyl-phenylamino)-N-(tetrahydropyran-2-yloxy)-benzamide;
3,4-Difluoro-2-(4-bromo-2-methyl-phenylamino)-N-(3-phenylprop-2-nyloxy)-benzamide;

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3,4-Difluoro-2-(4-bromo-2-methyl-phenylamino)-N-(3-furylmethoxy)-benzamide;
3,4-Difluoro-2-(4-bromo-2-methyl-phenylamino)-N-(2-thienylmethoxy)-benzamide;
3,4-Difluoro-2-(4-bromo-2-methyl-phenylamino)-N-(but-3-ynylmethoxy)-benzamide;
3,4-Difluoro-2-(4-bromo-2-methyl-phenylamino)-N-(2-methyl-prop-2-enyloxy)-benzamide;
3,4-Difluoro-2-(4-bromo-2-methyl-phenylamino)-N-(but-2-enyloxy)-benzamide;
3,4-Difluoro-2-(4-bromo-2-methyl-phenylamino)-N-(methoxy)-benzamide;
3,4-Difluoro-2-(4-bromo-2-methyl-phenylamino)-N-(ethoxy)-benzamide;
3,4-Difluoro-2-(4-bromo-2-methyl-phenylamino)-N-(cyclobutoxy)-benzamide;
3,4-Difluoro-2-(4-bromo-2-methyl-phenylamino)-N-(isopropoxy)-benzamide;
3,4-Difluoro-2-(4-bromo-2-methyl-phenylamino)-N-(2-phenoxyethoxy)-benzamide;
3,4-Difluoro-2-(4-bromo-2-methyl-phenylamino)-N-(cyclopropylmethoxy)-benzamide;
3,4-Difluoro-2-(4-bromo-2-methyl-phenylamino)-N-(n-propoxy)-benzamide;
3,4-Difluoro-2-(4-bromo-2-methyl-phenylamino)-N-(1-methyl-prop-2-ynylmethoxy)-benzamide;
3,4-Difluoro-2-(4-bromo-2-methyl-phenylamino)-N-(3-(3-fluorophenyl)-prop-2-ynylmethoxy)-benzamide;
3,4-Difluoro-2-(4-bromo-2-methyl-phenylamino)-N-(4,4-dimethylpent-2-ynylmethoxy)-benzamide;
3,4-Difluoro-2-(4-bromo-2-methyl-phenylamino)-N-(cyclopentoxy)-benzamide;
3,4,5-Trifluoro-N-hydroxy-2-(4-iodo-2-methyl-phenylamino)-benzamide;
5-Chloro-3,4-difluoro-N-hydroxy-2-(4-iodo-2-methyl-phenylamino)-benzamide;
5-Bromo-3,4-difluoro-2-(2-fluoro-4-iodo-phenylamino)-N-hydroxy-benzamide;
N-Hydroxy-2-(4-iodo-2-methyl-phenylamino)-4-nitro-benzamide;
3,4,5-Trifluoro-2-(2-fluoro-4-iodo-phenylamino)-N-hydroxy-benzamide;
5-Chloro-3,4-difluoro-2-(2-fluoro-4-iodo-phenylamino)-N-hydroxy-benzamide;
5-Bromo-2-(2-chloro-4-iodo-phenylamino)-3,4-difluoro-N-hydroxy-benzamide;
2-(2-Fluoro-4-iodo-phenylamino)-N-hydroxy-4-nitro-benzamide;
2-(2-Chloro-4-iodo-phenylamino)-3,4,5-trifluoro-N-hydroxy-benzamide;
5-Chloro-2-(2-chloro-4-iodo-phenylamino)-3,4-difluoro-N-hydroxy-benzamide;
5-Bromo-2-(2-bromo-4-iodo-phenylamino)-3,4-difluoro-N-hydroxy-benzamide;

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2-(2-Chloro-4-iodo-phenylamino)-N-hydroxy-4-methyl-benzamide;
2-(2-Bromo-4-iodo-phenylamino)-3,4,5-trifluoro-N-hydroxy-benzamide;
2-(2-Bromo-4-iodo-phenylamino)-5-chloro-3,4-difluoro-N-hydroxy-benzamide;
2-(2-Bromo-4-iodo-phenylamino)-N-hydroxy-4-nitro-benzamide;
4-Fluoro-2-(2-fluoro-4-iodo-phenylamino)-N-hydroxy-benzamide;
3,4-Difluoro-2-(2-fluoro-4-iodo-phenylamino)-N-hydroxy-benzamide;
2-(2-Chloro-4-iodo-phenylamino)-4-fluoro-N-hydroxy-benzamide;
2-(2-Chloro-4-iodo-phenylamino)-3,4-difluoro-N-hydroxy-benzamide;
2-(2-Bromo-4-iodo-phenylamino)-4-fluoro-N-hydroxy-benzamide;
2-(2-Bromo-4-iodo-phenylamino)-3,4-difluoro-N-hydroxy-benzamide;
N-Cyclopropylmethoxy-3,4,5-trifluoro-2-(4-iodo-2-methyl-phenylamino)-benzamide;
5-Chloro-N-cyclopropylmethoxy-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-benzamide;
5-Bromo-N-cyclopropylmethoxy-3,4-difluoro-2-(2-fluoro-4-iodo-phenylamino)-benzamide;
N-Cyclopropylmethoxy-2-(4-iodo-2-methyl-phenylamino)-4-nitro-benzamide;
N-Cyclopropylmethoxy-3,4,5-trifluoro-2-(2-fluoro-4-iodo-phenylamino)-benzamide;
5-Chloro-N-cyclopropylmethoxy-3,4-difluoro-2-(2-fluoro-4-iodo-phenylamino)-benzamide;
5-Bromo-2-(2-chloro-4-iodo-phenylamino)-N-cyclopropylmethoxy-3,4-difluoro-benzamide;
N-Cyclopropylmethoxy-2-(2-fluoro-4-iodo-phenylamino)-4-nitro-benzamide;
2-(2-Chloro-4-iodo-phenylamino)-N-cyclopropylmethoxy-3,4,5-trifluoro-benzamide;
5-Chloro-2-(2-chloro-4-iodo-phenylamino)-N-cyclopropylmethoxy-3,4-difluoro-benzamide;
5-Bromo-2-(2-bromo-4-iodo-phenylamino)-N-ethoxy-3,4-difluoro-benzamide;
2-(2-Chloro-4-iodo-phenylamino)-N-ethoxy-4-nitro-benzamide;
2-(2-Bromo-4-iodo-phenylamino)-N-cyclopropylmethoxy-3,4,5-trifluoro-benzamide;
2-(2-Bromo-4-iodo-phenylamino)-5-chloro-N-cyclopropylmethoxy-3,4-difluoro-benzamide
2-(2-Bromo-4-iodo-phenylamino)-N-cyclopropylmethoxy-4-nitro-benzamide;

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N-Cyclopropylmethoxy-4-fluoro-2-(2-fluoro-4-iodo-phenylamino)-benzamide;
N-Cyclopropylmethoxy-3,4-difluoro-2-(2-fluoro-4-iodo-phenylamino)-benzamide;
2-(2-Chloro-4-iodo-phenylamino)-N-cyclopropylmethoxy-4-fluoro-benzamide;
2-(2-Chloro-4-iodo-phenylamino)-N-cyclopropylmethoxy-3,4-difluoro-benzamide;
2-(2-Bromo-4-iodo-phenylamino)-N-cyclopropylmethoxy-4-fluoro-benzamide; and
2-(2-Bromo-4-iodo-phenylamino)-N-cyclopropylmethoxy-3,4-difluoro-benzamide.

14. (Previously Amended): The method of claim 1, comprising a MEK inhibitor having a structure selected from:

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2-(2-chloro-4-iodophenylamino)-5-chloro-N-cyclopropylmethoxy -3,4-difluorobenzamide;
2-(4-iodophenylamino)-N-cyclopropylmethoxy-5-chloro-3,4-difluorobenzamide;
2-(4-iodophenylamino)-5-chloro-3,4-difluorobenzoic acid;
2-(2-chloro-4-iodophenylamino)-5-chloro-3,4-difluorobenzoic acid;
5-chloro-3,4-difluoro-2-(4-ido-2-methylphenylamino)-benzoic acid; and
5-chloro-N-cyclopropylmethoxy -3,4-difluoro-2-(4-ido-2-methylphenylamino)-benzamide .

15. (Previously Amended): A method of treating or preventing arthritis in a patient in need of treatment, or suspected of developing arthritis, said method comprising the step of administering an effective antiarthritic amount of a compound selected from:

2-(2-Chloro-4-iodophenylamino)-N-cyclopropylmethoxy-3,4-difluorobenzamide;
2-(2-Methyl-4-iodophenylamino)-N-hydroxy-4-fluorobenzamide;
2-(2-Methyl-4-iodophenylamino)-N-hydroxy-3,4-difluoro-5-bromobenzamide;
2-(2-Methyl-4-iodophenylamino)-N-cyclopropylmethoxy-3,4-difluoro-5-bromobenzamide;
2-(2-Methyl-4-iodophenylamino)-N-cyclobutylmethoxy-3,4-difluoro-5-bromobenzamide;
2-(2-Chloro-4-iodophenylamino)-N-cyclopropylmethoxy-3,4-difluoro-5-bromobenzamide;

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2-(2-Chloro-4-iodophenylamino)-N-hydroxy-3,4-difluoro-5-bromobenzamide;
2-(2-Chloro-4-iodophenylamino)-N-cyclobutylmethoxy-3,4-difluorobenzamide;
2-(2-Chloro-4-iodophenylamino)-N-hydroxy-4-fluorobenzamide;
2-(2-Methyl-4-iodophenylamino)-N-hydroxy-3,4-difluorobenzamide;
2-(2-Methyl-4-iodophenylamino)-N-cyclopropylmethoxy-3,4,5-trifluorobenzamide; and
2-(2-Chloro-4-iodophenylamino)-N-cyclopropylmethoxy-4-fluorobenzamide.

16. (Previously Amended): The method of Claim 15 wherein said compound is selected from
2-(2-chloro-4-iodophenylamino)-N-cyclopropylmethoxy-3,4-difluorobenzamide;
2-(2-Methyl-4-iodophenylamino)-N-cyclopropylmethoxy-3,4,5-trifluorobenzamide; and
2-(2-Chloro-4-iodophenylamino)-N-cyclopropylmethoxy-4-fluorobenzamide.

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17. (Previously Added): A method of treating or preventing reducing the risk of arthritis in a patient in need of treatment, or suspected of developing arthritis, said method comprising the step of administering an effective antiarthritic amount of 2-(2-Chloro-4-iodophenylamino)-N-cyclopropylmethoxy-3,4-difluorobenzamide.

18. (Previously Added): The method of Claim 8, wherein the MEK inhibitor is a compound of Formula (I) wherein: Z is COOR₇; R₇ is H, pentafluorophenyl, or tetrazolyl; and R₃, R₄, and R₅ are independently H, fluoro, or chloro.

19. (Previously Added): The method of Claim 8, wherein the MEK inhibitor is a compound of Formula (I) wherein: Z is COOR₇; R₇ is H, pentafluorophenyl, or tetrazolyl; and R₃, R₄, and R₅ independently are fluoro.